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14. ABSTRACT

Purpose: The primary purposes of this study were to determine the effectiveness of Qu kClot Combat Gauze (QCG) and BleedArrest in a normovolemic model. In addition, the purposes were to investigate the effectiveness of QCG in a hemodiluted and resuscitated model; in a hypothermic model; and movement model. **Design**: Studies were prospective, experimental design. **Methods**: Swine were randomly assigned to experimental groups (normovolemic; resuscitated; hemodiluted after bleed; increased systolic blood pressure; hypothermic) or to a control group for each of the experimental groups. To simulate a trauma injury, the investigators generated a complex groin injury with transection of the femoral artery and vein in all pigs. After 1 minute of uncontrolled hemorrhage, the hemostatic agent was placed into the wound followed by standard wound packing. The control group underwent the same procedures with the exception of the hemostatic agent. In all groups, 5 minutes of direct manual pressure was applied to the wound followed by a standard pressure dressing. After 30 minutes, dressings were removed, and the amount of bleeding was determined. In the case of hemodilution, up to 5 liters of fluid were administered after hemostatis; in the case of prior hemodilution, 30% pigs' blood volume was exsanguinated, and a 3:1 ratio was administered; in the case of hypothermia, a temperature < 36 degrees C was achieved; and in the case of movements, the number of extremity movements were counted before rebleeding occurred. **Sample**: Yorkshire swine. **Analysis**: MANOVA was used. **Findings**: In all the studies (normovolemic; hemodiluted; resuscitated; hypothermic; and manipulation of systolic blood pressure, and movement of extremities, QCG was effective in hemorrhage control ($p < 0.05$). **Implications for Military Nursing**: QCG is effective in hemorrhage control. Our studies support the decision of the military to use QCG as the first-line hemostatic agent for use in treatment of severe hemorrhage.

15. SUBJECT TERMS
Hemorrhage control, vessel arterial and venous bleeding, hemostatic agent, hypothermic model

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Abstract

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Design: Studies were prospective, experimental design.

Methods: Swine were randomly assigned to experimental groups (normovolemic; resuscitated; hemodiluted after bleed; increased systolic blood pressure; hypothermic) or to a control group for each of the experimental groups. To simulate a trauma injury, the investigators generated a complex groin injury with transection of the femoral artery and vein in all pigs. After 1 minute of uncontrolled hemorrhage, the hemostatic agent was placed into the wound followed by standard wound packing. The control group underwent the same procedures with the exception of the hemostatic agent. In all groups, 5 minutes of direct manual pressure was applied to the wound followed by a standard pressure dressing. After 30 minutes, dressings were removed, and the amount of bleeding was determined. In the case of hemodilution, up to 5 liters of fluid were administered after hemostatis; in the case of prior hemodilution, 30% pigs' blood volume was exsanguinated, and a 3:1 ratio was administered; in the case of hypothermia, a temperature < 36 degrees C was achieved; and in the case of movements, the number of extremity movements were counted before rebleeding occurred.

Sample: Yorkshire swine

Analysis: MANOVA was used.

Findings: In all the studies (normovolemic; hemodiluted; resuscitated; hypothermic; and manipulation of systolic blood pressure, and movement of extremities, QCG was effective in hemorrhage control ($p < 0.05$).

Implications for Military Nursing: QCG is effective in hemorrhage control. Our studies support the decision of the military to use QCG as the first-line hemostatic agent for use in treatment of severe hemorrhage.

TSNRP Research Priorities that Study or Project Addresses

Primary Priority

Force Health Protection:	☐ Fit and ready force ☒ Deploy with and care for the warrior ☐ Care for all entrusted to our care
Nursing Competencies and Practice:	☒ Patient outcomes ☐ Quality and safety ☐ Translate research into practice/evidence-based practice ☐ Clinical excellence ☐ Knowledge management ☐ Education and training
Leadership, Ethics, and Mentoring:	☐ Health policy ☐ Recruitment and retention ☐ Preparing tomorrow's leaders ☐ Care of the caregiver
Other:	☐

Secondary Priority

Force Health Protection:	☒ Fit and ready force ☐ Deploy with and care for the warrior ☐ Care for all entrusted to our care
Nursing Competencies and Practice:	☐ Patient outcomes ☐ Quality and safety ☐ Translate research into practice/evidence-based practice ☐ Clinical excellence ☐ Knowledge management ☐ Education and training
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Other:	☐

Progress Toward Achievement of Specific Aims of the Study or Project

Trauma is the leading cause of morbidity and mortality in both civilian and military populations with uncontrolled hemorrhage as the major cause of death.[1-5] During the recent conflicts in Iraq and Afghanistan, uncontrolled hemorrhage accounted for nearly 50% of battlefield deaths prior to evacuation.[6] Trauma continues exceeds all of the other causes of death combined in persons younger than 36 years of age.[7] Furthermore, significant blood loss predisposes individuals to hypothermia, coagulopathy, infection, acidosis and multiple organ failure. Therefore, early control of hemorrhage is essential for initial survival and also for optimal recovery.[8] The US military's Committee on Tactical Combat Casualty Care (CTCCC) is the group responsible for developing guidelines for the management of wounded military personnel. CTCCC recommends QuikClot Combat Gauze (QCG) (Z-Medica, Wallingford, CT) as the first-line hemostatic agent for use in treatment of severe hemorrhage that cannot be controlled by a tourniquet.[9] QCG is a kaolin-impregnated rayon/polyester hemostatic dressing that promotes clotting by activation of factor XII (FXII) and factor XI (FXI) of the intrinsic coagulation pathway.[10]

QCG has been found to be effective in controlling massive hemorrhage in normothermic swine.[11-20] However, 30% to 50% of trauma patients present with hypothermic.[21,22] This is problematic because hypothermia impairs coagulation. In a retrospective 12-month analysis, Arthurs found that 18% of combat trauma patient admitted at the 31st Combat Support Hospital in Iraq were hypothermic (temperature < 36 degrees C).[23] Limited data exists relative to the effectiveness of hemostatic agents when the patient is hypothermic. Gegel and colleagues investigated the effectiveness of QCG in a hypothermic, porcine model and found that the agent was effective compared to a standard pressure dressing control.[24]

Trauma and shock with systemic hypoperfusion are probably responsible for the development of coagulopathy.[7] Acidosis is a common occurrence in trauma leading to impairment of the function of plasma proteases and to an increased degradation of fibrinogen. Furthermore, fluid resuscitation may dilute the clotting factors; therefore, hemodilution may influence the effectiveness of hemostatic agents.[7] According to Brohi, coagulopathy is common in trauma patients and is augmented by hypothermia and hemodilution because of large amounts of IV fluid administration.[25] Investigators have found several hemostatic agents are effective in hemorrhage control but often fail following IV crystalloid resuscitation. The failure may result from hemodilution or an increase in blood pressure or a combination.[2,3] Few studies have investigated the effectiveness of hemostatic agents, specifically QCG in a hemodiluted or volume resuscitated state. In two separate studies, Johnson and colleagues found that QCG was effective in a resuscitated and hemodiluted state, but they did not initially examine the additional effects of hypothermia.[(10, 29)] Subsequently, Gegel and colleagues found that QCG was effective not only in hypothermia but also after IV resuscitation with 5 liters of crystalloid fluid. Initially, the researchers did not investigate the effects of prior hemodilution. The clot had already formed when resuscitation fluid was administered and may not accurately reflect the effects of QCG in the presence of hemodilution.[24] Subsequently, several studies suggest that QCG is effective in a hemodiluted state including prior dilution.[11,26,27]

Concerns relative to how robust the clot developed by QCG and whether movement may dislodge the clot. Many studies have investigated QCG in swine models that do not include the effects of movement. Movement would most likely occur because of the patient's pain or in a situation where the individual had to be moved out of harm's way or for evacuation. Subsequent studies have demonstrated that QCG is more effective than a control group when the arterial pressure is increased and extremity movements are manipulated. [19,26,28,29]

The aims of this study have been investigated extensively by the research team. The aims were as follows:

The revised aims of this study are as follows:

1. Determine the effects of QCG and BleedArrest on hemorrhage control.
2. Determine the effect of movement on hemorrhage control when QCG is used.
3. Determine the effects of 5 liters intravenous fluid infusion on rebleeding when QCG is used.
4. Determine the effect of hemodilution and fluid resuscitation on bleeding when QCG is used.
5. Determine the effect of hemodilution and fluid resuscitation on bleeding when QCG is used in a hypothermic (34 degrees C) and normothermic state
6. Determine the effects of arterial blood pressure and intravenous fluid infusion on rebleeding when QCG is used.
7. Determine the effects of QCG on hemorrhage control in subjects that are hypothermic.
8. Determine the effects of intravenous fluid and arterial blood pressure on rebleeding when QCG are used in subjects that are hypothermic

All of the findings of our investigations have been published in refereed journals. In addition, the results have been presented at numerous regional, national, and international conferences.

Findings related to each specific aim, research or study questions, and/or hypothesis:

The following are findings of the studies relative to aim 1:

1. Determine the effects of QuikClot Combat Gauze and BleedArrest on hemorrhage control.

Introduction: This part of study investigated the effects of BleedArrest, TraumaDex, and Celox, on hemorrhage control.

Methods: This was a prospective, experimental study using male Yorkshire swine. The pigs (n = 10 per group) were randomly assigned to the BleedArrest, TraumaDex, and Celox or control group. To simulate a trauma injury, the investigators generated a complex groin injury with transection of the femoral artery and vein in all pigs. After 1 minute of uncontrolled hemorrhage, the hemostatic agent was placed into the wound followed by standard wound packing. The control group underwent the same procedures with the exception of the hemostatic agent. In all groups, 5 minutes of direct manual pressure was applied to the wound followed by a standard pressure dressing. After 30 minutes, dressings were removed, and the amount of bleeding was determined.

Results: There were significant differences between the BleedArrest (mean = 21.2, SD ± 36.6 mL) TraumaDex (mean = 68, SD ± 103.5 mL) and Celox (mean = 18.l6, SD ± 41.6 mL) groups compared to Control Group (mean = 230, SD ± 154 mL) ($p < 0.05$). However, there were no statistically significant differences between BleedArrest, TraumaDex, and Celox groups ($p = 0.478$).

Conclusions: These agents were clinically superior at controlling hemorrhage compared to the standard pressure dressing in the control group.

The following are findings of the studies relative to aim 1 and 2:

1. Determine the effects of QuikClot Combat Gauze and BleedArrest on hemorrhage control.
2. Determine the effect of movement on hemorrhage control when QuikClot Combat Gauze is employed.

Introduction: The purpose of this part of study was twofold: (1) to examine the effectiveness of QCG compared to a control group and (2) investigate the effect of movement on hemorrhage control when QCG is used.

Methods: This was a prospective, experimental design employing an established porcine model of uncontrolled hemorrhage. The minimum number of animals (n = 11 per group) was used to obtain a statistically valid result.

Results: The determination of effect size for this experiment was based upon previous work. Using the data in previous studies, the investigators calculated a large effect size of 0.6. Using G-Power 3.00, an effect size of 0.6, a power of 0.80 and an alpha of 0.05, it was determined that a sample size of 11 swine per group (22 total) was needed for this study. There were no statistically significant differences between the groups in reference to the amount of initial 1 minute hemorrhage ($p = 0.544$): QCG group ranged from 149 to 1004 mL (mean = 654, SD ± 283 mL); control group ranged from100 to 992 mL (mean = 582, SD ± 259 mL). The activated clotting time (ACT), the body weights, core body temperatures, amount of 1 minute hemorrhage, arterial blood pressures, amount of blood volume, and the amount and percentage of total blood volume of the initial hemorrhage were analyzed using a multivariate ANOVA. There were no statistically significant differences between the groups ($p > 0.05$) indicating that the groups were equivalent on these parameters. The ACT was within normal limits for all subjects. A multivariate ANOVA was used to determine if there were significant differences in the groups relative to the amount of hemorrhage over a five-minute period and the number of movements before hemorrhage. There was a significant difference in the groups relative to the amount of hemorrhage ($p = 0.018$) and the number of movements ($p =0.001$). The amount of bleeding QCG group ranged from 0 to 514 mL (mean = 50, SD ± 154 mL); control group ranged from 0 to 1002 mL (mean = 351, SD ± 354 mL). The number of movements for the OCG group ranged from 3 to 40 (mean = 36.6 ± 11) and for control group ranged from 0 to 9 (mean = 0.9 ± 2.7).

Conclusion: QCG was superior to a control group relative to hemorrhage control and the number of movements that created a rebleed.

The following are findings of the studies relative to aims 1, 2, and 3

1. Determine the effects of QuikClot Combat Gauze and BleedArrest on hemorrhage control.
2. Determine the effect of movement on hemorrhage control when QuikClot Combat Gauze is employed.
3. Determine the effects of 5 liters intravenous fluid infusion on rebleeding when QuikClot Combat Gauze is used.

Introduction: The purposes of this study were compare the effectiveness of QCG compared to a control group on hemorrhage control; the amount of crystalloid volume infusion on rebleeding; and the effect of movement on hemorrhage.

Methods: This was a prospective, experimental design. Swine were randomly assigned to either the QCG (n = 11) or the control group (n = 11). Investigators transected the femoral artery and vein in each swine. After one minute of uncontrolled hemorrhage, the hemostatic agent, QCG, was placed into the wound followed by standard wound packing. The control group underwent the same procedures but without a hemostatic agent. After five minutes of direct pressure, a standard pressure dressing was applied. After 30 minutes, dressings were removed, and the wound was observed for rebleeding for 5 minutes. If hemostasis occurred, 5 liters of crystalloid were given over 5 minutes, and the wound was observed for rebleeding for 5 additional minutes. If no bleeding occurred, the extremity on the side of the injury was moved.

Results: There were no statistically significant differences between the groups in reference to the amount of initial 1 minute hemorrhage ($p = 0.544$): QCG group ranged from 149 to 1004 mL (mean = 654, SD ± 283 mL); control group ranged from100 to 992 mL (mean = 582, SD ± 259 mL). There were no statistically significant differences between the groups (p 0.83) on ACT, the body weights, core body temperatures, amount of 1 minute hemorrhage, arterial blood pressures, amount of blood volume, the amount of the NPO fluid deficit replacement, and the amount and percentage of total blood volume indicating that the groups were equivalent on these parameters. The ACT was within normal limits for all subjects. There were significant differences in the groups relative to the amount of hemorrhage over a 5 minute period, amount of resuscitation fluid, and the number of movements before hemorrhage ($p = 0.004$). The amount of bleeding in the QCG group ranged from 0 to 514 mL (mean = 50, SD ± 154 mL); control group ranged from 0 to 1002 mL (mean = 351, SD ± 354 mL). The amount of resuscitation fluid in the QCG group ranged from 3000 to 5000 mL (mean = 4818, SD ± 603 mL); the control group ranged from 0 to 3000 mL (mean = 209, SD ± 600 mL). The number of movements for the OCG group ranged from 3 to 40 (mean = 36.6, SD ± 11) and for control group ranged from 0 to 9 (mean = 0.9, SD ± 2.7). A post-hoc Tukey was used to determine where the significance was. There was a significant difference in the groups relative to the amount of hemorrhage ($p = 0.018$), the amount of resuscitation fluid before rebleeding ($p < 0.001$), and the number of movements ($p < 0.001$).

Conclusion: The clinical implications are that QCG is effective in controlling hemorrhage, provides greater latitude in administration of resuscitation fluid, and provides confidence that clots formed with the agent allows movement without rebleeding.

The following are findings of the studies relative to aim 4:

4. Determine the effect of hemodilution and fluid resuscitation on bleeding when QuikClot Combat Gauze is used.

Introduction: Although hemostatic agents may be effective at stopping hemorrhage, they may fail because of hemodilution from intravenous fluids. The purpose of this part study was to investigate the effects of QCG on rebleeding in a class II hemorrhage in the presence of hemodilution in a lethal femoral injury.

Methods: This was a prospective experimental, between swine subjects design. Pigs were assigned to one of two groups: QCG (n=11) or control (n=11). Thirty percent of the pig's blood was exsanguinated and then a 3:1 ratio of ringers lactate was administered. A groin injury was created by transecting the femoral artery and vein to simulate a battlefield injury and allowed to bleed for one minute. After one minute of hemorrhage, proximal pressure was applied to the injury, and QCG was placed into the wound followed by standard wound packing. The control group underwent the same procedures with the exception of the hemostatic agent. For both groups, 5 minutes of direct pressure was applied to the wound followed by a standard pressure dressing. Dressings were removed after 30 minutes, and the amount of hemorrhage was calculated in milliliters for each group for a period of 5 minutes. An activated clotting time was used to exclude any pigs with coagulation pathology; all were within normal limits.

Results: A multivariate analysis of variance indicated that there were no significant differences in the groups relative to weight, amount of one minute hemorrhage, fluid deficit replacement, blood volume, and the activated clotting time ($p > .05$) indicating that the groups were equivalent on these parameters. A *t* test indicated that there was significantly less bleeding ($p = .002$) in the QCG group (36 mL±112 mL) compared to the control group (340 mL±297 ml).

Conclusion: QCG produces a robust clot that can more effectively tolerate hemodilution compared to a control group.

The following are findings of the studies relative to aims 2, 5 and aim 7:

2. Determine the effect of movement on hemorrhage control when QuikClot Combat Gauze is employed.
5. Determine the effect of hemodilution and fluid resuscitation on bleeding when QuikClot Combat Gauze is used in a hypothermic (34 degrees C) and normothermic state
7. Determine the effects of QuikClot Combat Gauze on hemorrhage control in subjects that are hypothermic.

Aims: The purposes of this part of the study were threefold; compare the QCG to a control group on hemorrhage control in a porcine model of hypothermia, investigate the effect of intravenous volume resuscitation on rebleeding, and the effect of movement on hemostasis.

Design: This was a prospective, between subjects, experimental design. Twenty-two Yorkshire swine were randomly assigned to two groups: QCG (n = 11) or control (n= 11).

Methods: The femoral artery and vein were transected. After 1 minute of uncontrolled hemorrhage, the hemostatic agent QCG was placed into the wound followed by standard wound packing. The control group underwent the same procedures without QCG. After 5 minutes of manual pressure at 25 pounds per square inch, a pressure dressing with an overlying 10 lb. sandbag was applied. Initial resuscitation was performed with 500 mL of rapidly administered IV 6% Hetastarch. Following 30 minutes of observation, the dressings were removed and any additional blood loss was collected and total blood loss calculated. Hemostasis was defined as < 2% total blood volume or ~ 100 mL in a 70 kg swine. If hemostasis occurred, 5 Liters of IV crystalloid were rapidly administered, and the wound was again observed for rebleeding. If no bleeding occurred, the extremity on the side of the injury was systematically moved through flexion, extension, abduction and adduction sequentially 10 times or until rebleeding occurred.

Results: All results are reported using mean ± standard deviation. There were no statistically significant differences between the groups relative to the amount of 1 minute hemorrhage ($p = .45$). The One minute hemorrhage in the QCG group ranged from 288 to 1798 mL (718 ± 442 mL) and the control group ranged from 407 to 2260 mL (882 ± 544 mL). There was no significant difference in temperature before the hemorrhage phase between the 2 groups ($p = .23$). The temperature for the QCG group ranged from 31.9 to 33.4º C (32.8 ± .50 º C) Temperature in the control group ranged from 32.3 and 34.0 º C (33.5 ± .54 º C). The activated clotting time (ACTs), body weights, core body temperatures, amount of 1 minute hemorrhage, arterial blood pressures, estimated blood volume, amount of NPO fluid deficit, and the amount and percentage of total blood volume of the initial hemorrhage were analyzed using a multivariate analysis of variance (MANOVA). There were no statistically significant differences in pre-interventional data between the groups ($p = .05$) indicating all groups were equivalent relative to these parameters. The pre-intervention ACT was within normal limits for all subjects. (See table 1 for a summary of one and five minutes by group)

Table 1: Summary of Hemorrhage for One and Five Minutes by Group

Time	Groups	Range	Means and Standard Deviations	P Values
One Minute Hemorrhage	QCG Group	288-1798 mL	718 ± 442 mL	No significant difference (P = 0.45)
	Control	407- 2260 mL	882 ± 544 mL	
Five Minute Hemorrhage	QCG Group	0-216 mL	24 ± 65 mL	Control significantly larger than GCG (P = .01*)
	Control	0-780 mL	414 ± 310 mL	

*Significance < 0.01

A MANOVA was used to determine if there were significant differences between the groups relative to the amount of hemorrhage over a 5 minute period, the volume of IV crystalloid fluid infused, and the number of movements before rebleeding. The MANOVA indicated a significant difference between the groups, Wilk's Lambda ($p = .01$). A Tukey's post-hoc test was

used to determine where the significance differences were. There were significant differences in the groups relative to the amount of hemorrhage (p = .01), the volume of IV crystalloid fluid infused before rebleeding (p= .01), and the number of movements before rebleeding (p =.03).

See Tables 1-3 for summary of results. The amount of bleeding in the QCG group ranged from 0 to 216 mL (24 ± 65 mL). The control group ranged from 0 to 780 mL (414 ± 310 mL). The amount of volume infused in the QCG group ranged from 0 to 5000 mL (4545 ± 1507 mL) The amount of volume infused in the control group ranged from 0 to 5000 mL (1364 ± 2335 mL). The number of movements for the QCG group ranged from 0 to 40 (29 ± 18.6), and the control group ranged from 0 to 40 (10.9 ± 18.6). (See table 2 and 3 for a summary of the amount of resuscitation fluid and movements relative to rebleeding)

Table 2: Summary of Amount of Resuscitation Fluid before Rebleeding

Groups	Range	Means and Standard Deviations	P Values
QCG Group	0 to 5000 mL	4545 ± 1507 mL	QCG group significantly larger than control (P = .01)*
Control	0 to 5000 mL	1364 ± 2335 mL	

*Significance < 0.01

Table 3 Summary of Extremity Movements before Rebleeding

Groups	Range	Means and Standard Deviations	P Values
QCG Group	0 to 40	29 ± 18.6	QCG Group significantly higher than control (P = .03)*
Control	0 to 40	10.9 ± 18.6	

*Significance < 0.05

Conclusion: Under hypothermic conditions, QCG is effective, clinically and statistically superior at controlling hemorrhage, allows for greater fluid resuscitation, and tolerates significant movement without rebleeding compared to the standard pressure dressing control.

The following are findings of the studies relative to aims 6 and 8.

6. Determine the effects of arterial blood pressure and intravenous fluid infusion on rebleeding when QuikClot Combat Gauze is used.
8. Determine the effects of intravenous fluid and arterial blood pressure on rebleeding when QuikClot Combat Gauze are used in subjects that are hypothermic

Introduction: The aims of the study were to: 1) determine the effectiveness of QCG; 2) determine the arterial blood pressure at which rebleeding occurs; 3) determine how much

intravenous fluid could be administered before hemorrhage reoccurred and 4) determine the number extremity movement on rebleeding when QCG was used. **Design:** This was a prospective, randomized, experimental study.

Methods: Adult Yorkshire pigs were randomly assigned to two groups QCG (n = 10) or control (n = 10). This study was a prospective, between subjects, experimental design using a porcine model. The study was approved by the Institutional Animal Care and Use Committee (IACUC), and the animals received care in compliance with the Animal Welfare Act. Using *G-Power 3.00*, an effect size of 0.6, a power of 0.80 and an alpha of 0.05, it was determined a sample size of 20 (10 swine per group) were needed to perform this study. Twenty adult, male Yorkshire swine weighing between 70 kg and 87 kg were assigned to 1 of 2 groups (n=10 per group), QCG or the control group by the use of computer- generated random numbers. This weight range represents the average weight of the US Army soldier. All swine were purchased from the same vendor and from the same lot number to avoid variability between subjects. Male pigs were used to avoid potential hormonal effects on coagulation. They were fed a standard porcine diet and observed for 3 days prior to determine good health. They remained NPO after midnight the day of the experiment except for water. Each animal received an intramuscular injection of ketamine (20 mg/kg) and atropine (0.04 mg/kg), placed supine on a field litter on top of the operating room table, and administered inhaled isoflurane (4% to 5%) for endotracheal intubation. After the swine were intubated, isoflurane was subsequently decreased to 1% to 2% isoflurane for the remainder of the experiment. The animals were ventilated (tidal volume 8-10 mL/kg) with a Narkomed 2B anesthesia machine, (Dräger Medical, Telford, PA). An 18 G angio-catheter was inserted to the auricular vein for peripheral intravenous access. The left carotid artery was cannulated with a 20 G catheter using a cut-down technique for continuous arterial blood pressure monitoring. A right central venous catheter was inserted using the modified Seldinger technique for central venous pressure monitoring. Heart rate, arterial blood pressure, electrocardiogaphy, oxygen saturation, end tidal CO_2, and rectal temperature were continuously monitored using a Marquette Solar 800 monitor system (GE Marquette Medical Systems, Milwaukee, WI). All catheters were continuously flushed with 0.9% saline solution (5 mL/hour) to maintain patency. The investigators created a complex groin injury, as described by Alam and colleagues, to simulate a penetrating, traumatic battlefield injury. Specifically, the proximal thigh soft tissues (skin, quadriceps, and adductor muscles) were dissected to expose the femoral artery and vein below the inguinal ligament within the femoral crease.[30] Subjects were stabilized for 30 minutes prior to beginning the experiment. An Activated Clotting Time (ACT) test was performed to screen all subjects for preexisting coagulopathy. Body temperature was maintained using a forced-air warming blanket if the temperature of the animal fell below 36 degrees Celsius. After the stabilization period, the investigators used a scalpel to simultaneously transect the femoral artery and vein. Each animal was allowed to bleed for 1 minute, simulating the expected response time of a tactical health care provider. Shed blood was collected with a suction catheter held within the wound distal to the transected vessels. After 1 minute of uncontrolled hemorrhage, proximal pressure was applied to the transected vessels and 4" X 4" gauze was used to blot excess blood from the wound per manufacturer's guidelines. In the QCG group, the hemostatic gauze was placed in the wound followed by an overlying layer of petroleum gauze to prevent adhesion of the QCG to the wound packing for later removal. Standard wound packing using Kerlex roller gauze (Covidien, Mansfield, MA.) was placed on top of the petroleum gauze layer until the wound cavity was filled. Five minutes of manual

pressure at 25 pounds per square inch (psi) was applied as measured by a TIF scale, (TIF Industries, Owatonna, MN). The scale was placed between the litter and operating room table directly under the wound site of the animal. The TIF scale (Model 9010A) is an electronic scale capable of measuring pressure exertion. The TIF instrument is precise within 0.05 ounces and accurate within 0.5%. The scale was zeroed with 1 investigator applying pressure while another observed the scale to ensure that manual pressure was maintained at 25 ± 0.5 ounces psi for 5 minutes. The purpose for using the TIF scale was to ensure manual pressure held on the wound was reproducible and consistently maintained from animal to animal. All times were measured with a stopwatch that was precise to 0.01 of a second and accurate within ± 0.1 of a second. The standard dressing control group received the same treatment with the exception of the use of QCG. The CoTCCC recommends that after 5 minutes of firm pressure, a pressure dressing should be applied.[31] A pressure dressing was simulated by the use of a 10 pound sand bag placed over the dressing for an additional 30 minutes. The investigators acknowledge a sand bag would not be available or used on the battlefield; however, the investigators used this method to maintain consistency and reproducibility from animal to animal. Hextend (Hospira, Inc., Lake Forest, IL), 500 mL, was administered as recommended by TCCC guidelines, consistent with current battlefield fluid resuscitation practice. After a total of 35 minutes of wound pressure (5 minutes of manual pressure and 30 minutes with a sand bag), the dressings were carefully removed to avoid disturbing the established clot, and the wound was observed for hemorrhage.

The operational definition of hemostasis for this study was clot formation with a blood loss of less than 2% of the swine's total blood volume over a 5 minute period. The total blood volume of swine is 70 mL/kg and is the same as an adult human male. If hemostasis were obtained, a phenylephrine infusion was initiated and titrated to increase the systolic blood pressure (SBP) by 10 mm Hg every 3 minutes to test the robustness of the newly formed clot. Each manipulation of SBP was maintained for 3 minutes while observing for rebleeding. If rebleeding (≥ 2 % of the swine's total blood volume) occurred, the administration of the drug was terminated and SBP at which rebleeding occurred was recorded. If no rebleeding occurred, the SBP continued to be increased until tachyphylaxis was observed and the SBP could not be increased regardless of the amount of phenylephrine used. This phenomenon was noted by the investigators to occur once the SBP reached approximately 200 mm Hg. The investigators note that phenylephrine would not be used in this resuscitation scenario. Rather, it was chosen for use as a tool to manipulate the SBP because the drug is a direct and selective alpha-1 agonist and commonly used in clinical anesthesia practice. Because of its selective mechanism of action, the drug is easily titratable. Further, the drug can easily reproduce the manipulation of blood pressures from subject to subject.

If no bleeding occurred during induced hypertension, the investigators further challenged the clot by rapidly administering 5 liters of IV lactated ringer's solution, and the wound was again observed for rebleeding for 5 minutes. If no rebleeding occurred, the lower extremity on the side of the injury was sequentially moved through 10 repetitions of full flexion, extension, abduction, and adduction until rebleeding occurred or range of movement testing was completed. The wound was again observed for rebleeding for 5 minutes. The amount of hemorrhage was calculated on 4 occasions: the initial injury, after dressing removal, during and after the use of phenylephrine, during and after the fluid resuscitation, and during and after range of motion testing periods. Total blood loss was calculated by weighing the absorbent pads placed

underneath the animals, all dressings, and the suction canister before and after each hemorrhage event.

Results and Discussion: The ACT results, body weights, body temperatures, total blood volume, 1 minute hemorrhage volume, and the percentage of total blood volume of the initial hemorrhage were analyzed using multivariate analyses of variance (MANOVA). There were no statistically significant differences between the groups (Wilks' Lambda, $p = 0.855$) indicating that the groups were equivalent on these parameters. All of the ACT specimens were within normal limits ruling out any pre-existing coagulopathy. A MANOVA was used to determine if there were significant differences between the groups relative to 5 minute hemorrhage, SBP, mean arterial pressure (MAP), amount of resuscitation fluid, and extremity movement. There was no significant difference between the 2 groups relative to the 1 minute hemorrhage. However, a significant difference between the 2 groups was noted relative to 5 minute hemorrhage in which QCG had significantly less hemorrhage than the control. Fisher's Exact Test indicated that that QCG was much more effective than the control relative to initial success of hemorrhage control, prevention of rebleeding following both induced hypertension and large volume fluid resuscitation, and absence of rebleeding following active range of motion testing ($p = .0001$). None of the swine in the QCG group rebled. Only 1 animal in the control group did not rebleed. All subjects in the QCG maintained hemostasis with elevated SBP compared to none in the control All subjects in the QCG group were able to tolerate 5000 mL of IV crystalloid fluid administration without rebleeding. No animals in the control group were able to receive the full 5000 mL of IV fluid without rebleeding. Further, only 1 animal was able to receive 2000 mL before rebleeding (Table 4). The QCG group was able to withstand more movement than the control (Table 5). All results are presented in mean ± standard deviation. Significance is indicated by a p value < 0.05.

Table 4. Summary of Hemorrhage at 1 and 5 Minutes

Time	Group	Range	Mean ± SD	P value
1 Minute Hemorrhage	QCG	212 - 1004 mL	725 ± 253 mL	No significant difference between groups (p = .298)
	Control	100 - 992 mL	602 ± 265 mL	
5 Minute Hemorrhage	QCG	0 - 40 mL	4 ± 12.6 mL	Significantly less hemorrhage in the QCG group compared to the control group (p = .003)
	Control	0 - 1002 mL	386 ± 352 mL	

Table 5. Summary of Highest Systolic Blood Pressure Achieved

Group	Range	Mean ± SD	P value
QCG	200 - 220 mm Hg	207 ± 7.3 mm Hg	QCG reached significantly higher SBP than control group (p = .0001)
Control	78 - 112 mm Hg	94 ± 12 mm Hg	

A summary of the highest MAP is summarized in table 6. The amount of resuscitation fluid administered is summarized in table 7 and the amount of extremity movements are summarized in table 8.

Table 6. Summary of the Highest Mean Arterial Blood Pressure Achieved

Group	Range	Mean ± SD	P value
QCG	96 - 215 mm Hg	172 ± 31 mm Hg	QCG group reached significantly higher MAP than control (p = .0001)
Control	53 - 91 mm Hg	75 - 14 mm Hg	

Table 7. Summary of Amount of Resuscitation Fluid Administered

Group	Range	Means ± SD	P value
QCG	0 - 5000 mL	5000 ± 0 mL	QCG group received significantly larger amount of fluid compared to the control (p = .0001)
Control	0 - 2000 mL	600 ± 966 mL	

Table 8. Summary of Lower Extremity Movements before Rebleeding Occurred

Group	Range	Mean ± SD	P value
QCG	3 – 40	36 ± 12	QCG group tolerated significantly more movements than control (p = .0001)
Control	0 - 9	1 ± 2.8	

Conclusions: The results of this part of the study strongly support that QCG is highly effective in managing uncontrolled, massive hemorrhage compared to a standard pressure dressing in this porcine model of penetrating, traumatic injury. Data from this study indicate when QCG is used, there is a decreased risk of rebleeding secondary to crystalloid infusion potentially allowing more latitude in fluid resuscitation. Further, increases in systolic and mean blood pressure are better tolerated. Specifically, clots formed with QCG are more robust and less likely to fail as a result of the elevation of systolic blood pressure and mean arterial pressure that occurs during injury, treatment and evacuation due to endogenous catecholamine release secondary to pain. Lastly, the results demonstrate the clot formed by QCG is capable of withstanding severe movement without rebleeding compared to a standard pressure dressing. Based on this the findings of this study, QCG is an effective hemostatic agent for use in trauma management. QCG is superior in controlling hemorrhage compared to standard pressure dressings. Also, the agent provides for greater latitude in increases in the systolic blood pressure, fluid resuscitation, and movement compared to a control group.

The following are findings of the studies relative to aims 2, 3, 7, and 8.

2. Determine the effect of movement on hemorrhage control when QuikClot Combat Gauze is used.
3. Determine the effects of 5 liters intravenous fluid infusion on rebleeding when QuikClot Combat Gauze is used.
4. Determine the effect of hemodilution and fluid resuscitation on bleeding when QuikClot is used.
7. Determine the effects of QuikClot Combat Gauze on hemorrhage control in subjects that are hypothermic.
8. Determine the effects of intravenous fluid and arterial blood pressure on rebleeding when QuikClot Combat Gauze are used in subjects that are hypothermic

Introduction: The purpose of this study was to compare the effectiveness QCG to a control group relative to movements on a porcine model with hemodilution and hypothermia.

Design: This was a prospective, between subjects, experimental design. Twenty-six York-shire swine were randomly assigned to two groups: QCG (n=13) or control (n=13).

Methods: The subjects were exsanguinated 30% of the blood volume; hypothermia was induced to for 10 minutes. The hemostatic agent, QCG, was placed into the wound followed by standard wound packing. If the hemostasis was achieved, 5 Liters of IV crystalloid were rapidly administered, and the wound was again observed for rebleeding. If no bleeding occurred, the extremity on the side of the injury was systematically moved thorough flexion, extension, abduction and adduction sequentially 10 times or until rebleeding occurred.

Results: There were no statistically differences between the groups in reference to the amount of initial 1 minute hemorrhage, body weight, core body temperatures, arterial blood pressure, pulse, MAP, blood volume, amount of fluid resuscitation, or the amount of initial hemorrhage ($p=0.292$). Fluid replacement mean was 4454.86mL (4338.18 ± 673.48 in QCG group, 4571.55 ± 750.32 control group). Temperature was 33.31 Celsius, (33.05 ± 0.64 QCG group, 33.57± 0.34 control group). The ACT was within normal limits for all subjects. After 5L fluid challenge, hemostasis was achieved in all of the QCG group vs. 2 in the control group (100% vs. 15%). This means that 13 subjects had their extremities moved in the QCG group; 11 subjects had bleeding with no movement in the control group. An independent t-test was used to determine if there were statistically significant differences in the number of movements before hemorrhage occurred. The QCG group was able to tolerate movements more than the control group ($p <.0001$). See table 9 for a summary of the number of extremity movements before rebleeding.

Table 9: Summary of extremity movements before rebleeding.

Group	n of movements	p value
QCG	32.92 ± 14.062	<.0001
Control	6.15 ± 15.021	<.0001

Discussion: QCG is currently used by the US military and in many civilian sectors of management of massive hemorrhage in trauma casualties. The US military's Committee on Tactical Casualty Care is responsible for developing guidelines for the management of wounded military personnel. It recommends QCG as the first-line hemostatic agent for use in treatment of severe hemorrhage. The findings on this study support the recommendations. One goal of the US Army's is that each soldier carries and hemostatic agent. QCG produces a robust clot that can withstand significant movement. The movements were completed to a maximum range of motion and should be avoided in patients with an inguinal injury. However, the investigators wanted reproducible movements that would test the robustness of newly formed clot. Additional studies should be implemented investigating the effectiveness of QCG with immediate movement.

Relationship of current findings to previous findings:

The findings of our studies are consistent with other studies. Trabatonni and colleagues found that QCG obtained prompt hemostasis and allowed for early ambulation without clinical complications when the agent was used after coronary diagnostic and intervention procedures.[32] In a study by Politi, he and his colleagues found that QCG can reduce bleeding after diagnostic or interventional procedures.[33] Inaba compared the efficacy of QCG, Celox and Celox Gauze versus a standard gauze in a high-grade liver injury. The Celox products caused several deaths because of bowel obstruction. The authors concluded that QCG was effective and created durable hemostasis.[34] Satterly and colleagues investigated the effects of Celox, ChitoGauze, QCG and HemCon bandages applied to arterial injuries and concluded that QCG was the most effective and was rated the easiest dressing to use by soldiers.[35] Causey investigated the efficacy of QCG in a model of severe acidosis and coagulopathy to mimic a posttraumatic environment. QCG significantly outperformed standard gauze dressing in this extreme physiological model of a vascular injury.[36] In 2010, Kheirabadi found that the use of QCG had less hemorrhage and resulted in the highest survival rate compared to Trauma Stat, Celox and HemCon and a standard pressure dressing.[14]

Effect of problems or obstacles on the results:

There were few problems relative to the studies. On two occasions, staff members of University of Texas Health Science Center were ill making it difficult to collect data in a timely fashion. However, the staff was very accommodating to schedule additional days for data collection. On three occasions, there were not enough swine and the data collection days had to be canceled. Other days were available but the schedule of the team members had to be adjusted to accommodate data collection.

Initially, the investigators had difficulty in achieving hypothermia in this part of the study. This was overcome by applying cold alcohol spray to each swine and then using a fan to accelerate hypothermia. After changing the procedures, this was not an issue. Another issue was making them too hypothermic. We observed the core body temperature and as soon as each pig reached hypothermia, the study was implemented. However, not all swine had the same temperature but there were no significant differences in the groups relative to this parameter.

Scheduling with all of the investigators and the staff at University of Texas Health Science Center was sometimes difficult causing delays in data collection. On three occasions, pigs scheduled for the study were accidently fed. Rescheduling was required and did create a problem with the study having enough staff. The staff members at University of Texas Health Science Center were able to take over the duties of our staff without any difficulty.

We had difficulty in acquiring Hextend. All of the vendors required a physician's order. We eventually acquired a prescription from a local physician and went to a local pharmacy to get the Hextend. After this episode, we used University of Texas Health Science Center to acquire the fluid. Although it was more costly, it was well worth the extra funds.

To save funds, we purchased all of our supplies and transported to the laboratory. There was no place to store all of the supplies. Transporting the supplies back and forth became problematic but we were able to implement the studies without difficulty.

We considered these problems to be minor. The investigators were able to complete the study accomplishing all of the aims.

Limitations:

The results of this study may not be generalizable to humans. However, the circulatory systems, blood volume, and clotting cascade are very similar making this an excellent hemostatic model.[37]

The investigators thought about blinding the data collectors. We decided this would be very difficult and would add little rigor to the study. It was clear when we packed the wound with standard dressing and when QCG was used; therefore, we decided not to blind the investigators. We were concerned about experimenter effect. For the most part, we able to have the same individual investigator implement the same procedures. In some instances, this was not possible because of scheduling, but most procedures were routine and followed guidelines that it did not matter who was implementing the procedure. The PI of the study directed all activities and made sure that all procedures were followed in the same manner.

Another limitation was related to transecting the femerol artery and vein. At the end of each experiment, the investigators examined these vessels to make sure both were transected. In one of the model development animals, we found that the artery was transected but the vein was not. To prevent this from reoccurring, we use a scalpel that was shaped with the cutting edge at the top. The scalpel was turned to the side to guide it under both artery and vein. Both vessels were visible over the scalpel. During the transecting process, the scalpel was turned so the cutting edge was facing upward. We did not have any additional problems but to make sure both the vessels were transected, we examined each pig after the experiment was complete and all swine did have both vessels transected.

All of the equipment worked well. On a few occasions, we were unable to collect data relative to cardiac output, stroke volume, and arterial blood pressure. However, this accounted for only about ten minutes of data collection time and not at critical times.

Conclusion:

QCG and BleedArrest were effective in controlling hemorrhage. QCG allowed more movement before rebleeding compared to a control group. In addition, QCG allowed for latitude in intravenous fluid administration: the agent was more effective than a control when 5 liters were administered. We also found that in a hemodiluted state, QCG was more effective in controlling hemorrhage and that more fluid could be administered than a control before rebleeding occurred. Furthermore, we found that QCG was more effective in a hypothermic state than a control group. Also, we found that the clot was robust as evidenced by a higher systolic blood pressure being achieved before rebleeding occurred.

1. Determine the effects of QuikClot Combat Gauze and BleedArrest on hemorrhage control.
2. Determine the effect of movement on hemorrhage control when QuikClot Combat Gauze is employed.
3.
4. Determine the effects of 5 liters intravenous fluid infusion on rebleeding when QuikClot Combat Gauze is used.
5. Determine the effect of hemodilution and fluid resuscitation on bleeding when QuikClot is used.
6. Determine the effect of hemodilution and fluid resuscitation on bleeding when QuikClot Combat Gauze is used in a hypothermic (34 degrees C) and normothermic state
7. Determine the effects of arterial blood pressure and intravenous fluid infusion on rebleeding when QuikClot Combat Gauze is used.
8. Determine the effects of QuikClot Combat Gauze on hemorrhage control in subjects that are hypothermic.
9. Determine the effects of intravenous fluid and arterial blood pressure on rebleeding when QuikClot Combat Gauze are used in subjects that are hypothermic

Significance of Study or Project Results to Military Nursing

Trauma is the leading cause of morbidity and mortality in both civilian and military populations with uncontrolled hemorrhage as the major cause of death.[1-5] During the recent conflicts in Iraq and Afghanistan, uncontrolled hemorrhage accounted for nearly 50% of battlefield deaths prior to evacuation.[6] Trauma continues exceeds all of the other causes of death combined in persons younger than 36 years of age.[7] Furthermore, significant blood loss predisposes individuals to hypothermia, coagulopathy, infection, acidosis and multiple organ failure. Therefore, early control of hemorrhage is essential for initial survival and also for optimal recovery.[8] CTCCC recommends QCG as the first-line hemostatic agent for use in treatment of severe hemorrhage that cannot be controlled by a tourniquet.[9] However, at the time that the recommendation, there were limited data relative to the effectiveness of QCG. Our studies addressed concerns relative to the effectiveness of QCG in controlling hemorrhage, effectiveness in a resuscitation model, effectiveness of the agent in a hypovolemic model, the robustness of the clot, and whether the clot could withstand movement. The results have been consistent in that QCG was superior to a standard dressing in hemorrhage control. Our study supports the decision that QCG be used as the first-line agent for treatment of soldiers who are hemorrhaging.

Changes in Clinical Practice, Leadership, Management, Education, Policy, and/or Military Doctrine that Resulted from Study or Project

The primary purposes of this study were to determine the effectiveness of QuikClot Combat Gauze (QCG) and BleedArrest in a normovolemic model. In addition, the purposes were to investigate the effectiveness of QCG in a hemodiluted and resuscitated model; in a hypothermic model; and movement model. In all the studies (normovolemic; hemodiluted; resuscitated; hypothermic; and manipulation of systolic blood pressure, and movement of extremities, QCG was effective in hemorrhage control ($p < 0.05$).

QCG is currently used by the US military for management of massive hemorrhage in trauma casualties. The CTCCC recommends QCG as the first-line hemostatic agent for use in treatment of severe hemorrhage. However, there have been limited data demonstrating the effectiveness of QCG as a hemostatic agent. Clinicians and researchers have emphasized the metabolic benefit of replenishing the oxygen debt with volume resuscitation accumulated during hemorrhage. These benefits must be weighed against the deleterious effects of rebleeding. Continuing hemorrhage associated with rebleeding results in increased complications, morbidity and mortality. The US military and the CTCCC advocate permissive hypotension. Specifically, the use of low-volume resuscitation in trauma casualties until definitive hemorrhage control is achieved. The investigators found that QCG produced a more robust clot maintaining hemorrhage control during fluid resuscitation and movement compared to a standard pressure dressing in both a normal and hypothermic model.

QCG meets the necessary requirements for hemostatic agents for civilian and military use. The qualities include the ability to rapidly stop large vessel arterial and venous bleeding within 2 minutes through a pool of blood; no requirement for mixing or pre-application preparation; simplicity of application; light weight and durable; long shelf life greater than 2 years in extreme environments; safe to use with no risk of injury to tissues or transmission of infection ; and inexpensive. Based on the results of our studies, the military has made the appropriate choice in recommending QCG as the first-line hemostatic agent.

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Summary of Dissemination

Type of Dissemination	**Citation**	**Date and Source of Approval for Public Release**
Publications	Gegel, B., Burgert, J., Cooley, B., MacGregor, J., Myers, J., Calder, S., . . . Johnson, D. (2010). The effects of BleedArrest, Celox, and TraumaDex on hemorrhage control in a porcine model. *J Surg Res, 164*(1), e125-129. doi: 10.1016/j.jss.2010.07.060	6/20/2015 4/27/2015
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Poster Presentations	Burgert J, Gegel B, Johnson D. (2008). The Effects of Arterial Blood Pressure on Rebleeding when Celox and TraumaDex are Used in a Porcine Model of Lethal Femoral Injury. Karen Rieder Research Poster Session. San Antonio, TX. **Second place award**. Gegel B, Burgert J, Johnson D. (2008). The Effects of Celox and TraumaDex on Hemorrhage Control in a Porcine Model. Karen Rieder Research Poster Session. San Antonio, TX. Gegel B, Burgert J, Johnson D. (2009). The Effects of Celox and TraumaDex on Hemorrhage Control and Rebleeding in a Porcine Model. Pacific Institute of Nursing Conference. Honolulu, HI. Gegel B, Burgert J, Johnson D. (2009) The Effects of Arterial Blood Pressure on Rebleeding when Celox and TraumaDex are used in a Porcine Model of Lethal Femoral Vascular Injury. AANA Annual Meeting. San Diego, CA. Burgert J, Gegel B, Johnson A. (2010). The Effects of Arterial Blood Pressure on Rebleeding when BleedArrest, Celox and TraumaDex are used in a Porcine Model of	

	Lethal Femoral Injury. Podium Presentation. AANA Annual Meeting. Seattle, WA. Gegel, B, Johnson, D, Burgert, J, Loughren, J. and Johnson, D. The Effects of BleedArrest and QuikClot on Hemorrhage Control in a Porcine Model, Battlefield Summit, April, 2010, San Antonio, TX Gasko J, B Gegel B, Burgert, J, Johnson, D. The Effects of Hemostatic Agents on Hemorrhage Control in a Porcine Model, Battlefield Medicine Symposium, March, 2010, Washington, DC Gasko J, Burgert J, Gegel, B. (2011) The Effects of BleedArrest on Hemorrhage Control in a Porcine Model. Poster Presentation. AANA Annual Meeting. Boston, MA. Brennan A, Gegel B, Burgert J. (2011) The Effects of Fluid Resuscitation on Rebleeding When BleedArrest is used in a Porcine Model of Lethal Femoral Injury. Podium Presentation. AANA Annual Meeting. Boston, MA. Gegel B, Burgert J, Johnson D. (2011). The Effects of BleedArrest on Hemorrhage Control in a Porcine Model of Lethal Femoral Injury. Poster Presentation. AMSUS Annual Meeting. San Antonio, TX. Gegel B, Burgert J, Johnson D. (2012) The Effects of QuikClot Combat Gauze and Movement on Hemorrhage Control in a Porcine Model. Poster presentation. AANA Annual Meeting. San Francisco, CA. Agee S, Johnson D, Burgert J. (2012) The Effects of QuikClot Combat Gauze on Hemorrhage Control in the Presence of Hemodilution. Podium and poster presentation. Monanalua, HI Gegel B, Burgert J, Johnson D. (2012) The Effects of QuikClot Combat Gauze and Movement on Hemorrhage Control in a Porcine Model. Poster presentation. TANA Fall Meeting. Gegel B, Burgert J, Johnson D. (2012) The Effects of QuikClot Combat Gauze and Movement on Hemorrhage Control in a Porcine Model. Poster presentation. Army Nurse Corps Association Conference. San Antonio, TX. San Antonio, TX. Gegel B, Burgert J, Johnson D. (2012) The Effects of QuikClot Combat Gauze and Movement on Hemorrhage Control in a Porcine Model. Poster presentation. Army	

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Media Reports	None	
Other	None	

Reportable Outcomes

Reportable Outcome	Detailed Description
Applied for Patent	None
Issued a Patent	None
Developed a cell line	None
Developed a tissue or serum repository	None
Developed a data registry	None

Recruitment and Retention Aspect	Number
Animals Projected in Grant Application	164
Animals Purchased	152
Model Development Animals	4
Research Animals	152
Animals With Complete Data	152
Animals with Incomplete Data	0